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Appl. No. 10/656,098
Reply to Office Action of July 20, 2006

REMARKS/ARGUMENTS

The claims remain rejected as anticipated or obvious over Inoue et al. (US 5,635,308), either as a primary reference or a secondary reference. Inoue is relied on in each rejection for its disclosure of compounds meeting the claim requirements (including the rejection over Tanaka in view of Inoue). The issues still revolve around the meaning of the claims as distinguished from Inoue et al. In particular, the meaning of the "internal rotational isomerism," which is an important feature defining the compounds required by the invention.

Atropiosomerism (or internal rotational isomerism) is well known in the art. Enclosed herewith is a copy of relevant portions of K. Mislow, "Introduction To Stereochemistry" (1966).

Referring to Mislow, Figure 2-18 (on page 82), illustrated are variously substituted terphenyls to show that isomerism depends on the particular substitution pattern.

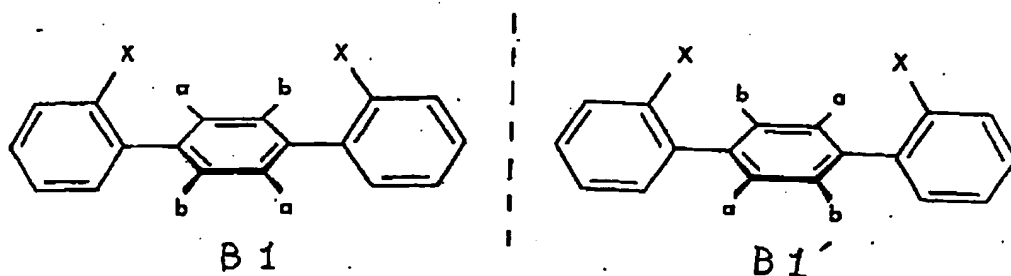
It is noted that in any of these terphenyls, rotation is hindered about a single bond between phenyl and phenylene nuclei. As described therein (last paragraph bridging pages 80-81), for

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example, in B the cis-form is dissymmetric, and gives rise to two enantiomers (or optically active d,l pair). On the contrary, the trans-form has S_2 symmetry and is therefore nondissymmetric, and gives rise to one meso-form. Thus, the trans-form does not exist in enantiomeric forms.

Alternatively, the cis-form (B1) and its mirror image (B1') are shown below. Clearly, the object and the mirror image are not superimposable and in the cis-form, therefore, two enantiomers that are stereoisomers resulting from hindered rotation about a single bond (i.e., internal rotational isomerism) exist.

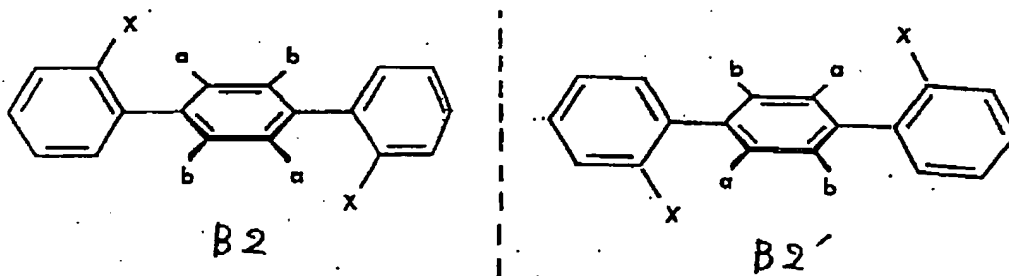


The trans-form (B2) and its mirror image (B2') are also shown below. As can be seen, the object and the mirror image are superimposable and therefore no enantiomeric isomerism arises, and therefore, only one meso-form exists in the trans-form.

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Thus, in the trans-form, rotation about a single bond is also hindered, but nevertheless, no enantiomeric isomerism exist.



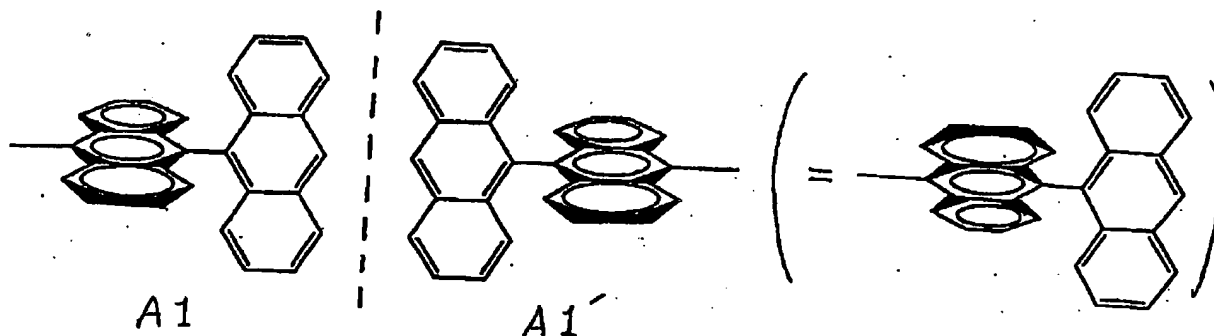
In applicants' response filed May 16, 2006, it is argued that with respect to the compound of formula A-16, all biaryl groups in the compound are 9,9'-bianthracene-10-yl groups, that free rotation about the 9,9'-bond is hindered, and mirror images that are not superimposable exist. With respect to a 9,9'-bianthracene-10,10'-diyl group such as in Inoue's Compound VII-21, it is argued that free rotation is hindered about the 9,9'-bond but the mirror images are superimposable, and therefore, it is submitted that the 9,9'-bianthracene-10,10'-diyl included in the Inoue's compound is not a biaryl group having a bond capable of giving an internal rotation isomerism.

Further, the foregoing 9,9'-bianthracene-10-yl and 9,9'-bianthracene-10,10'-diyl groups are also depicted as below.

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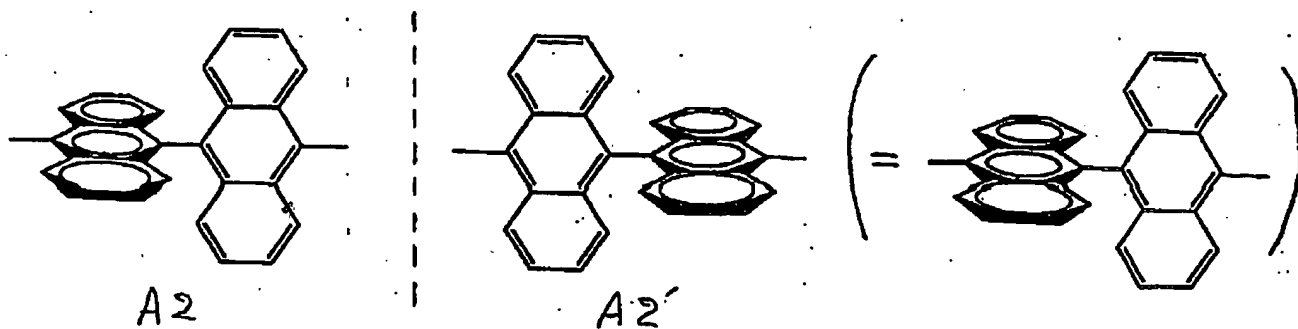
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A 9,9'-bianthracene-10-yl group (A1) and its mirror image (A1') are illustrated below:



As can be seen, the object (A1) and its mirror image (A1') are not superimposable and enantiomeric isomers. In other words, a 9,9'-bianthracene-10-yl group is dissymmetric and enantiomer forms exists, therefore, the 9,9'-bond of this 9,9'-bianthracene-10-yl group is a biaryl group giving an internal rotational isomerism.

On the other hand, a 9,9'-bianthracene-10,10'-diyl group (A2) and its mirror image (A2') are illustrated below:



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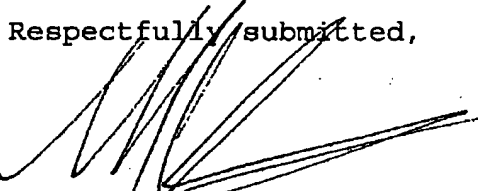
As can be seen, the object (A2) and its mirror image (A2') are superimposable and therefore, no enantiomer exists. Thus, the 9,9'-bond of this 9,9'-bianthracene-10,10'-diyl group is not a biaryl group giving an internal rotational isomerism.

In any event, based on the foregoing reasoning, it is submitted that the 9,9'-bianthracene-10,10'-diyl is not a biaryl group giving an internal rotational, therefore, Inoue does not teach nor suggest any compound falling within the scope of the present invention. Nor does Inoue support the features of the required compounds when combined with other art, to render the present invention obvious.

In view of the above, the anticipation and obviousness rejections are not supported by the art. Allowance of the application is therefore respectfully requested.

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Respectfully submitted,



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Enclosure: "INTRODUCTION TO STEREOCHEMISTRY," Kurt Mislow, 1966,
Princeton University, W.A. Benjamin, Inc.,
Amsterdam, NY

■ INTRODUCTION TO STEREOCHEMISTRY

KURT MISLOW PRINCETON UNIVERSITY

W. A. BENJAMIN, INC. ■ New York, Amsterdam

1966

80

■ INTRODUCTION TO STEREOCHEMISTRY

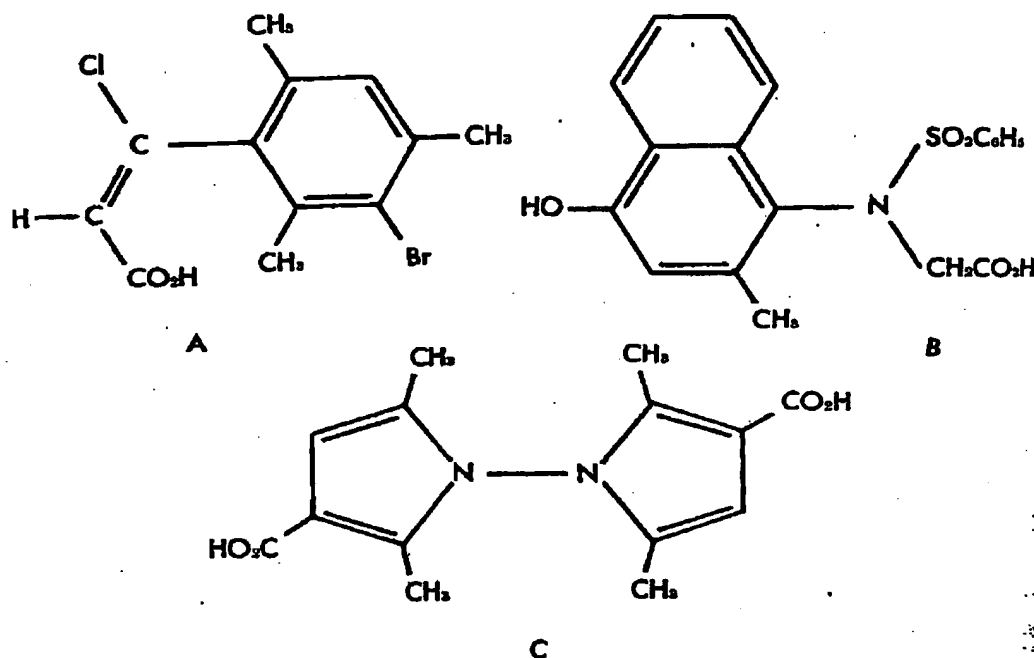


FIGURE 2-16

Some optically active compounds exhibiting biphenyl-like atropisomerism. Pivot bonds are marked in color. The planar conformations are overcrowded.

double bridging shown in Figure 1-16 is not essential; even a single bridge suffices, with or without blocking substituents (Figure 2-15).

The concept of biphenyl atropisomerism is readily extended to systems which differ formally in structure but in which the stereochemical requirements for atropisomerism closely resemble those in optically active biphenyls (Figure 2-16). However, the attribute of being "biphenyl-like" is not a necessary one for the condition of atropisomerism. For example, in tri-*o*-thymotide (Figure 1-15), the propeller-like (C_3) enantiomers rapidly interconvert at room temperature, but not so rapidly as to preclude polarimetric observation of this process. Atropisomerism has been demonstrated in a variety of other structural types (Figure 2-17).

Atropisomerism does not necessarily imply enantiomerism. The separate forms may instead be diastereomers. This is illustrated in Figure 2-18 for the case of variously substituted terphenyls. For each of the substitution patterns shown, the *cis*- and *trans*-forms are diastereomers, and additional isomerism depends on the particular substitution pattern. Thus in *A*, *cis*- and *trans*-forms are both dissymmetric and may therefore each exist in enantiomeric forms. In *B* the *cis*-form is dissymmetric (two enan-

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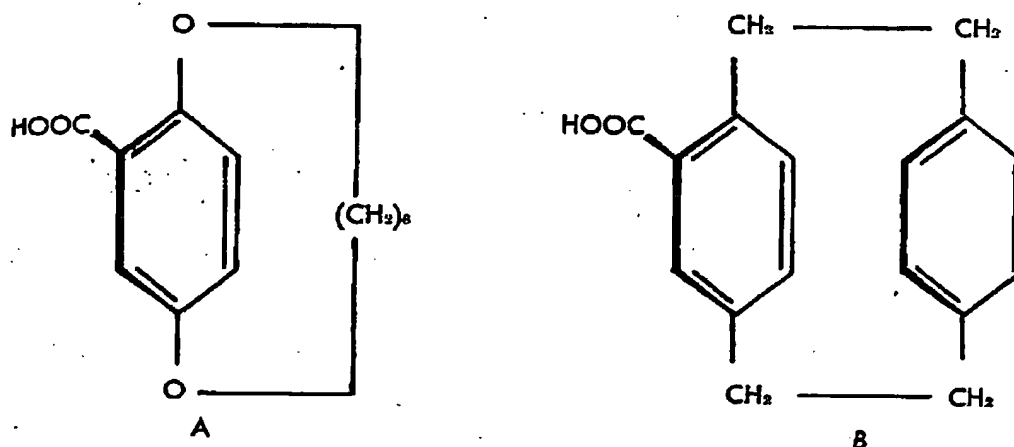


FIGURE 2-17

Examples of optically active atropisomers: A, an ansa compound; B, a paracyclophane. Pivot bonds are marked in color.

tiomers), but the *trans*-form has S_2 symmetry and is therefore non-dissymmetric and optically inactive (an optically inactive diastereomer is called a *meso*-form). In C it is the *trans* isomer which is dissymmetric whereas the *cis*-form is the *meso*-isomer (C_2), and in D both isomers are *meso* (*cis*- C_{2v} and *trans*- C_{2h}). In short: A has two *dl*-pairs, B and C have one *dl*-pair and one *meso*-form, and D has two *meso*-forms.

A restricted biphenyl has been prepared in enantiomerically homogeneous form in which the 2- and 2'-positions are occupied by $-\text{CH}_3$ groups, and the 6- and 6'-positions by $-\text{CD}_3$ groups. This compound, like ethyl-*n*-propyl-*n*-butyl-*n*-hexylmethane, is dissymmetric but exhibits no optical activity at any wave length, as measured with currently available spectropolarimeters: This illustrates the general principle that dissymmetry and enantiomeric homogeneity are no guarantee of measurable optical activity.

TORSIONAL DOUBLE BOND (GEOMETRIC) ISOMERISM The pivot bonds of geometric isomers, like those of conformational isomers, may be formed between two like or two unlike atoms (Figure 2-19). Other things being equal, these stereoisomers are separated by much higher energy barriers than single-bond isomers, for reasons discussed above (Sec. 1-5), and they are therefore usually quite stable at room temperature.

In principle, 2ⁿ diastereomers are possible for constitutionally unsymmetrical acyclic olefins with *n* double bonds, e.g., $\text{CH}_3\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{COOH}$ (*n* = 2), as illustrated in Table 2-1 for *n* = 1 to 4. This Table also introduces the term "configuration."

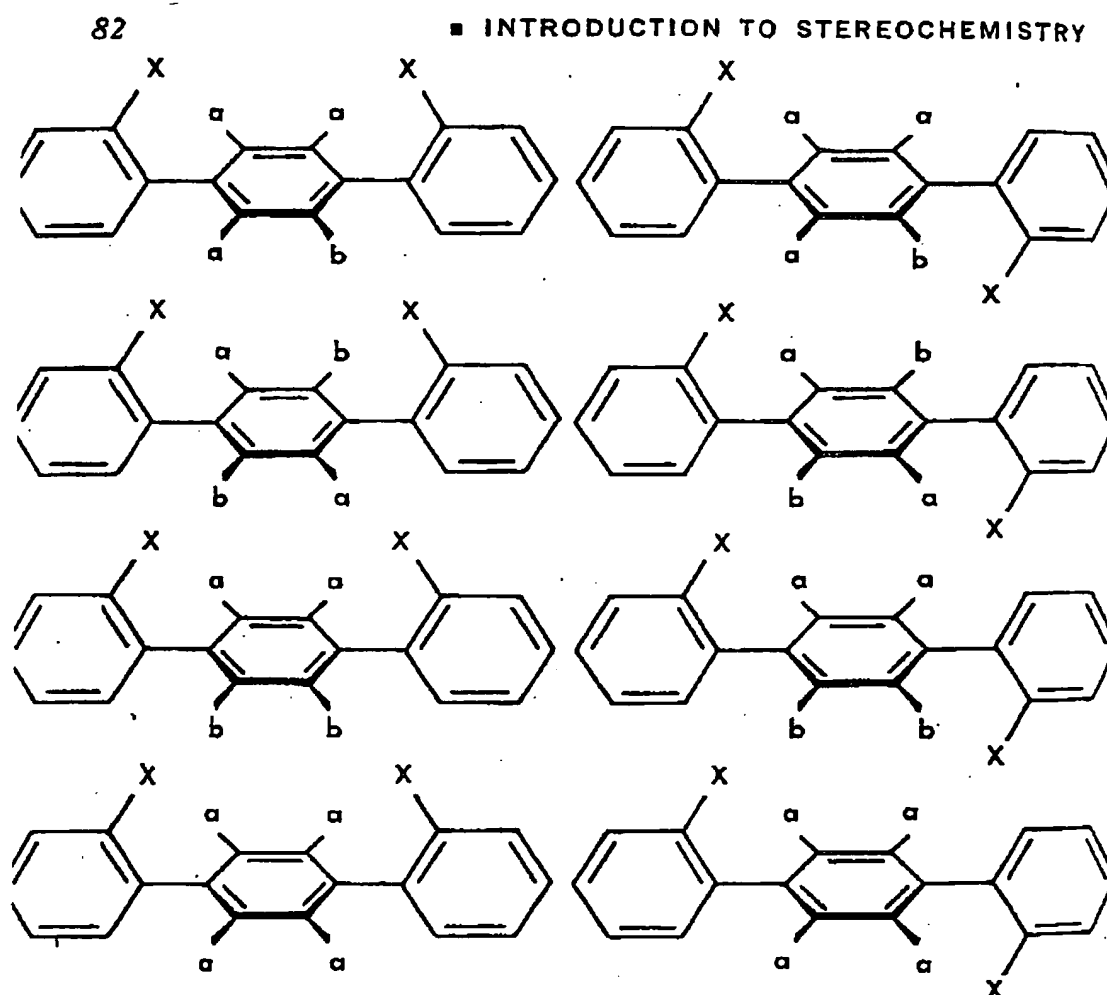


FIGURE 2-18

Atropisomerism in variously substituted terphenyls. The end rings are in the plane of the paper and the middle ring is at right angles to the other two. For a given substitution pattern A, B, C, or D, the formula on the left represents the cis and the one on the right the trans form.

By *configuration* we mean the relative position or order of the arrangement of atoms in space which characterizes a particular stereoisomer. For example, enantiomers differ characteristically in their configurations because their chiralities are opposite: Enantiomers have "opposite" configurations. Diastereomers have configurations which, though not opposite, are different. The designation of diastereomeric configurations generally presents no problem; in the present case the notations *cis* and *trans* in the Table refer to the configuration of the respective diastereomers.

Although the *trans*-isomer is generally the more stable form, the *cis*-isomer often predominates among naturally occurring non-conjugated fatty acids. For example, oleic, linoleic, linolenic, and